

SEQUENCE LISTING

<110> Robertson, David

Blakely, Randy D.

<120> GENETIC MUTATION UNDERLYING ORTHOSTATIC INTOLERANCE  
5 AND DIAGNOSTIC AND THERAPEUTIC METHODS RELATING THERETO

<130> Attorney Docket No. 1242-27-2-2

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<150> 60/175,456

10 <151> 2000-01-11

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<160> 40

<170> PatentIn Ver. 2.0

15 <210> 1

<211> 1854

<212> DNA

<213> Homo sapiens

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<221> CDS

<222> (1)..(1851)

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5 <301> Porzgen, P.

Bonisch, H.

Bruss, M.

<302> Molecular Cloning and Organization of the Coding Region  
of the Human Norepinephrine Tranporter Gene

10 <303> Biochem. Biophys. Res. Commun.

<304> 215

<305> (3)

<306> 1145-1150

<307> 1995

15 <308> x91117

<309> 1996-02-20

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Arg Phe Pro Tyr Leu Cys Tyr Lys Asn Gly Gly Gly Ala Phe Leu Ile  
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Tyr Tyr Leu Phe Ser Ser Phe Thr Leu Asn Leu Pro Trp Thr Asp Cys  
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Val Leu Phe Val Leu Leu Val His Gly Val Thr Leu Pro Gly Ala Ser  
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Asn Gly Ile Asn Ala Tyr Leu His Ile Asp Phe Tyr Arg Leu Lys Glu  
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		20	25	30
	Leu Leu Val Val Lys Glu Arg Asn Gly Val Gln Cys Leu Leu Ala Pro			
		35	40	45
	Arg Asp Gly Asp Ala Gln Pro Arg Glu Thr Trp Gly Lys Lys Ile Asp			
		50	55	60
30	Phe Leu Leu Ser Val Val Gly Phe Ala Val Asp Leu Ala Asn Val Trp			
		65	70	75
	Arg Phe Pro Tyr Leu Cys Tyr Lys Asn Gly Gly Gly Ala Phe Leu Ile			
		85	90	95
35	Pro Tyr Thr Leu Phe Leu Ile Ile Ala Gly Met Pro Leu Phe Tyr Met			
		100	105	110
	Glu Leu Ala Leu Gly Gln Tyr Asn Arg Glu Gly Ala Ala Thr Val Trp			
		115	120	125
	Lys Ile Cys Pro Phe Phe Lys Gly Val Gly Tyr Ala Val Ile Leu Ile			
		130	135	140
40	Ala Leu Tyr Val Gly Phe Tyr Tyr Asn Val Ile Ile Ala Trp Ser Leu			
		145	150	155
	Tyr Tyr Leu Phe Ser Ser Phe Thr Leu Asn Leu Pro Trp Thr Asp Cys			
		165	170	175
45	Gly His Thr Trp Asn Ser Pro Asn Cys Thr Asp Pro Lys Leu Leu Asn			
		180	185	190
	Gly Ser Val Leu Gly Asn His Thr Lys Tyr Ser Lys Tyr Lys Phe Thr			
		195	200	205

	Pro 210	Ala	Ala	Glu	Phe	Tyr	Glu 215	Arg	Gly	Val	Leu 220	His	Leu	His	Glu	Ser
	Ser 225	Gly	Ile	His	Asp	Ile 230	Gly	Leu	Pro	Gln	Trp 235	Gln	Leu	Leu	Leu	Cys 240
5	Leu	Met	Val	Val	Val 245	Ile	Val	Leu	Tyr	Phe 250	Ser	Leu	Trp	Lys	Gly 255	Val
	Lys	Thr	Ser	Gly 260	Lys	Val	Val	Trp	Ile 265	Thr	Ala	Thr	Leu	Pro 270	Tyr	Phe
10	Val	Leu	Phe 275	Val	Leu	Leu	Val	His 280	Gly	Val	Thr	Leu	Pro 285	Gly	Ala	Ser
	Asn 290	Gly	Ile	Asn	Ala	Tyr	Leu 295	His	Ile	Asp	Phe	Tyr 300	Arg	Leu	Lys	Glu
	Ala 305	Thr	Val	Trp	Ile	Asp 310	Ala	Ala	Thr	Gln	Ile 315	Phe	Phe	Ser	Leu	Gly 320
15	Ala	Gly	Phe	Gly	Val 325	Leu	Ile	Ala	Phe	Ala 330	Ser	Tyr	Asn	Lys	Phe 335	Asp
	Asn	Asn	Cys	Tyr 340	Arg	Asp	Ala	Leu	Leu 345	Thr	Ser	Ser	Ile	Asn 350	Cys	Ile
20	Thr	Ser	Phe 355	Val	Ser	Gly	Phe 360	Ala	Ile	Phe	Ser	Ile	Leu 365	Gly	Tyr	Met
	Ala 370	His	Glu	His	Lys	Val	Asn 375	Ile	Glu	Asp	Val	Ala 380	Thr	Glu	Gly	Ala
	Gly 385	Leu	Val	Phe	Ile	Leu 390	Tyr	Pro	Glu	Ala	Ile 395	Ser	Thr	Leu	Ser	Gly 400
25	Ser	Thr	Phe	Trp	Ala 405	Val	Val	Phe	Phe	Val 410	Met	Leu	Leu	Ala	Leu 415	Gly
	Leu	Asp	Ser	Ser 420	Met	Gly	Gly	Met	Glu 425	Ala	Val	Ile	Thr	Gly 430	Leu	Ala
30	Asp	Asp	Phe 435	Gln	Val	Leu	Lys 440	Arg	His	Arg	Lys	Leu 445	Phe	Thr	Phe	Gly
	Val	Thr	Phe 450	Ser	Thr	Phe	Leu 455	Leu	Pro	Leu	Phe	Cys 460	Ile	Thr	Lys	Gly
	Gly 465	Ile	Tyr	Val	Leu	Thr 470	Leu	Leu	Asp	Thr	Phe 475	Ala	Ala	Gly	Thr	Ser 480
35	Ile	Leu	Phe	Ala 485	Val	Leu	Met	Glu	Ala	Ile 490	Gly	Val	Ser	Trp	Phe 495	Tyr
	Gly	Val	Asp 500	Arg	Phe	Ser	Asn	Asp	Ile 505	Gln	Gln	Met	Met	Gly 510	Phe	Arg
40	Pro	Gly	Leu 515	Tyr	Trp	Arg	Leu	Cys 520	Trp	Lys	Phe	Val	Ser 525	Pro	Ala	Phe
	Leu	Leu	Phe 530	Val	Val	Val	Val 535	Ser	Ile	Ile	Asn	Phe 540	Lys	Pro	Leu	Thr
	Tyr 545	Asp	Asp	Tyr	Ile	Phe 550	Pro	Pro	Trp	Ala	Asn 555	Trp	Val	Gly	Trp	Gly 560
45	Ile	Ala	Leu	Ser	Ser 565	Met	Val	Leu	Val	Pro 570	Ile	Tyr	Val	Ile	Tyr 575	Lys

Phe Leu Ser Thr Gln Gly Ser Leu Trp Glu Arg Leu Ala Tyr Gly Ile  
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5 Phe Gln Leu Gln His Trp Leu Ala Ile  
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1 5 10 15

15

gcg gac acg ggt cca gag cag ccc ctt cgg gcg cgc aaa act gcg gag 96  
Ala Asp Thr Gly Pro Glu Gln Pro Leu Arg Ala Arg Lys Thr Ala Glu  
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ctg ctg gtg gtg aag gag cgc aac ggc gtc cag tgc ctg ctg gcg ccc 144  
Leu Leu Val Val Lys Glu Arg Asn Gly Val Gln Cys Leu Leu Ala Pro  
35 40 45

20

cgc gac ggc gac gcg cag ccc cgg gag acc tgg ggc aag aag atc gac 192  
Arg Asp Gly Asp Ala Gln Pro Arg Glu Thr Trp Gly Lys Lys Ile Asp  
50 55 60

25

ttc ctg ctg tcc gta gtc ggc ttc gca gtg gac ctg gcc aac gtg tgg 240  
Phe Leu Leu Ser Val Val Gly Phe Ala Val Asp Leu Ala Asn Val Trp  
65 70 75 80

cgc ttc ccc tac ctc tgc tac aag aac ggc ggc ggt gcc ttc ttg atc 288  
Arg Phe Pro Tyr Leu Cys Tyr Lys Asn Gly Gly Gly Ala Phe Leu Ile  
85 90 95

30

ccg tac aca ctg ttc ctt atc atc gcg ggg atg ccc ctg ttc tac atg 336  
Pro Tyr Thr Leu Phe Leu Ile Ile Ala Gly Met Pro Leu Phe Tyr Met  
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gag ctg gct ctg gga cag tac aac cgg gag ggg gct gcc acc gtt tgg 384  
Glu Leu Ala Leu Gly Gln Tyr Asn Arg Glu Gly Ala Thr Val Trp  
115 120 125

35

aaa atc tgc cca ttc ttc aaa ggc gtt ggc tat gct gtc atc ctg atc 432  
Lys Ile Cys Pro Phe Phe Lys Gly Val Gly Tyr Ala Val Ile Leu Ile  
130 135 140

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tac tac ctc ttc tcc tcc ttc acc ctc aac ctg ccc tgg acc gac tgt 528  
Tyr Tyr Leu Phe Ser Ser Phe Thr Leu Asn Leu Pro Trp Thr Asp Cys  
165 170 175

45

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Gly His Thr Trp Asn Ser Pro Asn Cys Thr Asp Pro Lys Leu Leu Asn  
180 185 190

ggc tcc gtg ctt ggc aac cac acc aag tac tcc aag tac aag ttc acg 624  
Gly Ser Val Leu Gly Asn His Thr Lys Tyr Ser Lys Lys Phe Thr  
195 200 205

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	Ser Gly Ile His Asp Ile Gly Leu Pro Gln Trp Gln Leu Leu Leu Cys	
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	ctg atg gtc gtc gtc atc gtc ttg tat ttt agc ctc tgg aaa ggg gtg	768
	Leu Met Val Val Val Ile Val Leu Tyr Phe Ser Leu Trp Lys Gly Val	
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10	aag aca tca gga aag gtg gtg tgg atc aca gcc acg ctg cct tac ttc	816
	Lys Thr Ser Gly Lys Val Val Trp Ile Thr Ala Thr Leu Pro Tyr Phe	
	260 265 270	
15	gtg ctg ttc gtg ctc ctg gtc cat ggc gtc acg ctg ccc gga gcc tcc	864
	Val Leu Phe Val Leu Leu Val His Gly Val Thr Leu Pro Gly Ala Ser	
	275 280 285	
	aat ggc atc aat gcc tac ctg cac atc gac ttc tac cgc ttg aaa gag	912
	Asn Gly Ile Asn Ala Tyr Leu His Ile Asp Phe Tyr Arg Leu Lys Glu	
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	Ala Thr Val Trp Ile Asp Ala Ala Thr Gln Ile Phe Phe Ser Leu Gly	
	305 310 315 320	
	gct gga ttt gga gta ttg att gca ttt gcc agt tac aac aaa ttt gac	1008
	Ala Gly Phe Gly Val Leu Ile Ala Phe Ala Ser Tyr Asn Lys Phe Asp	
	325 330 335	
25	aac aac tgt tac agg gat gcc ctg ctg acc agc agc atc aac tgt atc	1056
	Asn Asn Cys Tyr Arg Asp Ala Leu Leu Thr Ser Ser Ile Asn Cys Ile	
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30	acc agc ttc gtc tct ggg ttc gcc atc ttc tcc atc ctt ggt tac atg	1104
	Thr Ser Phe Val Ser Gly Phe Ala Ile Phe Ser Ile Leu Gly Tyr Met	
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	gcc cat gaa cac aag gtc aac att gag gat gtg gcc aca gaa gga gct	1152
	Ala His Glu His Lys Val Asn Ile Glu Asp Val Ala Thr Glu Gly Ala	
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35	ggc cta gtg ttc atc ctg tat cca gag gcc att tct acc ctg tct gga	1200
	Gly Leu Val Phe Ile Leu Tyr Pro Glu Ala Ile Ser Thr Leu Ser Gly	
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	tct aca ttc tgg gct gtt gtg ttt ttc gtc atg ctc ctg gcg ctg ggc	1248
	Ser Thr Phe Trp Ala Val Val Phe Phe Val Met Leu Leu Ala Leu Gly	
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40	ctt gac agc tca atg gga ggc atg gag gct gtc atc acg ggc ctg gca	1296
	Leu Asp Ser Ser Met Gly Gly Met Glu Ala Val Ile Thr Gly Leu Ala	
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	Asp Asp Phe Gln Val Leu Lys Arg His Arg Lys Leu Phe Thr Phe Gly	
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	gtc acc ttc agc act ttc ctt ctc gcc ctg ttc tgc ata acc aag ggt	1392
	Val Thr Phe Ser Thr Phe Leu Leu Ala Leu Phe Cys Ile Thr Lys Gly	
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50	gga att tac gtc ttg acc ctc ctg gac acc ttt gct gcg ggc acc tcc	1440
	Gly Ile Tyr Val Leu Thr Leu Leu Asp Thr Phe Ala Ala Gly Thr Ser	
	465 470 475 480	
	atc ctt ttt gct gtc ctc atg gaa gcc atc gga gtt tcc tgg ttt tat	1488

Ile Leu Phe Ala Val Leu Met Glu Ala Ile Gly Val Ser Trp Phe Tyr  
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Gly Val Asp Arg Phe Ser Asn Asp Ile Gln Gln Met Met Gly Phe Arg  
500 505 510

ccg ggt cta tac tgg aga ctg tgc tgg aag ttc gtc agt cct gcc ttc 1584  
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10 ctc ctg ttc gtg gtt gtg gtc agc atc atc aac ttc aag cca ctc acc 1632  
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Tyr Asp Asp Tyr Ile Phe Pro Pro Trp Ala Asn Trp Val Gly Trp Gly  
545 550 555 560

15 atc gcc ctg tcc tcc atg gtc ctg gtg ccc atc tac gtc atc tat aag 1728  
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20 ttc ctc agc acg cag ggc tct ctt tgg gag aga ctg gcc tat ggc atc 1776  
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580 585 590

acg cca gag aac gag cac cac ctg gtg gct cag agg gac atc aga cag 1824  
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35 40 45

Arg Asp Gly Asp Ala Gln Pro Arg Glu Thr Trp Gly Lys Lys Ile Asp  
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40 Phe Leu Leu Ser Val Val Gly Phe Ala Val Asp Leu Ala Asn Val Trp  
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Arg Phe Pro Tyr Leu Cys Tyr Lys Asn Gly Gly Gly Ala Phe Leu Ile  
85 90 95

45 Pro Tyr Thr Leu Phe Leu Ile Ile Ala Gly Met Pro Leu Phe Tyr Met  
100 105 110

Glu Leu Ala Leu Gly Gln Tyr Asn Arg Glu Gly Ala Ala Thr Val Trp  
115 120 125

Lys Ile Cys Pro Phe Phe Lys Gly Val Gly Tyr Ala Val Ile Leu Ile  
130 135 140

Ala Leu Tyr Val Gly Phe Tyr Tyr Asn Val Ile Ile Ala Trp Ser Leu  
145 150 155 160

Tyr Tyr Leu Phe Ser Ser Phe Thr Leu Asn Leu Pro Trp Thr Asp Cys  
165 170 175

5 Gly His Thr Trp Asn Ser Pro Asn Cys Thr Asp Pro Lys Leu Leu Asn  
180 185 190

Gly Ser Val Leu Gly Asn His Thr Lys Tyr Ser Lys Tyr Lys Phe Thr  
195 200 205

10 Pro Ala Ala Glu Phe Tyr Glu Arg Gly Val Leu His Leu His Glu Ser  
210 215 220

Ser Gly Ile His Asp Ile Gly Leu Pro Gln Trp Gln Leu Leu Leu Cys  
225 230 235 240

Leu Met Val Val Val Ile Val Leu Tyr Phe Ser Leu Trp Lys Gly Val  
245 250 255

15 Lys Thr Ser Gly Lys Val Val Trp Ile Thr Ala Thr Leu Pro Tyr Phe  
260 265 270

Val Leu Phe Val Leu Leu Val His Gly Val Thr Leu Pro Gly Ala Ser  
275 280 285

20 Asn Gly Ile Asn Ala Tyr Leu His Ile Asp Phe Tyr Arg Leu Lys Glu  
290 295 300

Ala Thr Val Trp Ile Asp Ala Ala Thr Gln Ile Phe Phe Ser Leu Gly  
305 310 315 320

Ala Gly Phe Gly Val Leu Ile Ala Phe Ala Ser Tyr Asn Lys Phe Asp  
325 330 335

25 Asn Asn Cys Tyr Arg Asp Ala Leu Leu Thr Ser Ser Ile Asn Cys Ile  
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Thr Ser Phe Val Ser Gly Phe Ala Ile Phe Ser Ile Leu Gly Tyr Met  
355 360 365

30 Ala His Glu His Lys Val Asn Ile Glu Asp Val Ala Thr Glu Gly Ala  
370 375 380

Gly Leu Val Phe Ile Leu Tyr Pro Glu Ala Ile Ser Thr Leu Ser Gly  
385 390 395 400

Ser Thr Phe Trp Ala Val Val Phe Phe Val Met Leu Leu Ala Leu Gly  
405 410 415

35 Leu Asp Ser Ser Met Gly Gly Met Glu Ala Val Ile Thr Gly Leu Ala  
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Asp Asp Phe Gln Val Leu Lys Arg His Arg Lys Leu Phe Thr Phe Gly  
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40 Val Thr Phe Ser Thr Phe Leu Leu Ala Leu Phe Cys Ile Thr Lys Gly  
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Gly Ile Tyr Val Leu Thr Leu Leu Asp Thr Phe Ala Ala Gly Thr Ser  
465 470 475 480

Ile Leu Phe Ala Val Leu Met Glu Ala Ile Gly Val Ser Trp Phe Tyr  
485 490 495

45 Gly Val Asp Arg Phe Ser Asn Asp Ile Gln Gln Met Met Gly Phe Arg  
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	Pro Gly 515	Leu Tyr 520	Trp Arg	Leu Cys 525	Trp Lys	Phe Val 525	Pro Ala 525	Phe	
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	Ile Ala 565	Leu Ser 565	Ser Met 570	Val Leu 570	Pro Ile 575	Tyr Val 575	Ile Tyr 575	Lys	
10	Phe Leu 580	Ser Thr 580	Gln Gly 585	Ser Leu 585	Trp Glu 590	Arg Leu 590	Ala Tyr 590	Gly Ile	
	Thr Pro 595	Glu Asn 595	Glu His 600	His Leu 600	Val Ala 605	Gln Arg 605	Asp Ile 610	Arg Gln	
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	gcg gac acg ggt cca gag cag ccc ctt cgg gcg cgc aaa act gcg gag 96	Ala Asp Thr Gly Pro Glu Gln Pro Leu Arg Ala Arg Lys Thr Ala Glu	20	25	30				
30	ctg ctg gtg gtg aag gag cgc aac ggc gtc cag tgc ctg gcg ccc 144	Leu Leu Val Val Lys Glu Arg Asn Gly Val Gln Cys Leu Leu Ala Pro	35	40	45				
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35	ttc ctg ctg tcc gta gtc ggc ttc gca gtg gac ctg gcc aac gtg tgg 240	Phe Leu Leu Ser Val Val Gly Phe Ala Val Asp Leu Ala Asn Val Trp	65	70	75				
40	cgc ttc ccc tac ctc tgc tac aag aac ggc ggc ggt gcc ttc ttg atc 288	Arg Phe Pro Tyr Leu Cys Tyr Lys Asn Gly Gly Gly Ala Phe Leu Ile	85	90	95				
	ccg tac aca ctg ttc ctt atc atc gcg ggg atg ccc ctg ttc tac atg 336	Pro Tyr Thr Leu Phe Leu Ile Ile Ala Gly Met Pro Leu Phe Tyr Met	100	105	110				
45	gag ctg gct ctg gga cag tac aac cgg gag ggg gct gcc acc gtt tgg 384	Glu Leu Ala Leu Gly Gln Tyr Asn Arg Glu Gly Ala Ala Thr Val Trp	115	120	125				
	aaa atc tgc cca ttc ttc aaa ggc gtt ggc tat gct gtc atc ctg atc 432	Lys Ile Cys Pro Phe Phe Lys Gly Val Gly Tyr Ala Val Ile Leu Ile							



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	ggc tcc gtg ctt ggc aac cac acc aag tac tcc aag tac aag ttc acg Gly Ser Val Leu Gly Asn His Thr Lys Tyr Ser Lys Tyr Lys Phe Thr 195 200 205	624		
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30	aat ggc atc aat gcc tac ctg cac atc gac ttc tac cgc ttg aaa gag Asn Gly Ile Asn Ala Tyr Leu His Ile Asp Phe Tyr Arg Leu Lys Glu 290 295 300	912		
	gcc acg gta tgg att gat gcc gca act cag ata ttt ttt tcc ttg ggg Ala Thr Val Trp Ile Asp Ala Ala Thr Gln Ile Phe Phe Ser Leu Gly 305 310 315 320	960		
35	gct gga ttt gga gta ttg att gca ttt gcc agt tac aac aaa ttt gac Ala Gly Phe Gly Val Leu Ile Ala Phe Ala Ser Tyr Asn Lys Phe Asp 325 330 335	1008		
40	aac aac tgt tac agg gat gcc ctg ctg acc agc agc atc aac tgt atc Asn Asn Cys Tyr Arg Asp Ala Leu Leu Thr Ser Ser Ile Asn Cys Ile 340 345 350	1056		
	acc agc ttc gtc tct ggg ttc gcc atc ttc tcc atc ctt ggt tac atg Thr Ser Phe Val Ser Gly Phe Ala Ile Phe Ser Ile Leu Gly Tyr Met 355 360 365	1104		
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	ggc cta gtg ttc atc ctg tat cca gag gcc att tct acc ctg tct gga Gly Leu Val Phe Ile Leu Tyr Pro Glu Ala Ile Ser Thr Leu Ser Gly 385 390 395 400	1200		
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5	gat gac ttc cag gtc ctg aag cga cac cgg aaa ctc ttc aca ttt ggc	1344
	Asp Asp Phe Gln Val Leu Lys Arg His Arg Lys Leu Phe Thr Phe Gly	
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	gtc acc ttc agc act ttc ctt ctc ccc ctg ttc tgc ata acc aag ggt	1392
	Val Thr Phe Ser Thr Phe Leu Leu Pro Leu Phe Cys Ile Thr Lys Gly	
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10	gga att tac gtc ttg acc ctc ctg gac acc ttt gct gcg ggc acc tcc	1440
	Gly Ile Tyr Val Leu Thr Leu Leu Asp Thr Phe Ala Ala Gly Thr Ser	
	465 470 475 480	
15	atc ctt ttt gct gtc ctc atg gaa gcc atc gga gtt tcc tgg ttt tat	1488
	Ile Leu Phe Ala Val Leu Met Glu Ala Ile Gly Val Ser Trp Phe Tyr	
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	gga gtg gac agg ttc agc aac gac atc cag cag atg atg ggg ttc agg	1536
	Gly Val Asp Arg Phe Ser Asn Asp Ile Gln Gln Met Met Gly Phe Arg	
	500 505 510	
20	ccg ggt cta tac tgg aga ctg tgc tgg aag ttc gtc agt cct gcc ttc	1584
	Pro Gly Leu Tyr Trp Arg Leu Cys Trp Lys Phe Val Ser Pro Ala Phe	
	515 520 525	
	ctc ctg ttc gtg gtt gtg gtc agc atc atc aac ttc aag cca ctc acc	1632
	Leu Leu Phe Val Val Val Val Ser Ile Ile Asn Phe Lys Pro Leu Thr	
	530 535 540	
25	tac gac gac tac atc ttc ccg ccc tgg gcc aac tgg gtg ggg tgg ggc	1680
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